How does a photocatalytic antimicrobial coating affect environmental bioburden in hospitals?

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SHORT TITLE

Evaluation of a photocatalytic coating on hospital surfaces

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Background:

The healthcare environment is recognized as a source for healthcare-acquired infection. Since cleaning practices are often erratic and always intermittent, it is postulated that continuously antimicrobial surfaces offer superior control of surface bioburden.

Objective:

This study evaluated the impact of a photocatalytic antimicrobial coating at near-patient high-touch sites in a hospital ward.

Setting:

Two acute wards in a large acute hospital.

Methods:

A titanium dioxide-based photocatalytic coating was sprayed onto six surfaces within a four-bed bay in a ward and compared against the same surfaces in an untreated ward, both under normal illumination. Sites were right and left bedrails; bed control; bedside locker, overbed table; and bed footboard. Overall microbial burden and presence of an indicator pathogen (*S. aureus*) were assessed biweekly using standardized methods for 12 weeks.

Results:

Treated surfaces demonstrated significantly lower microbial burden than control sites, with the difference increasing between treated and untreated surfaces during the study. Hygiene failures (>2.5 cfu/cm^2) increased 2.6% per day (OR=1.026; 95%CI 1.009 to 1.043; P = 0.003) for control surfaces but declined 2.5% per day for treated surfaces (OR=0.95; 95%CI 0.925 to 0.977; P < 0.001).There was no significant difference between coated and control surfaces regarding *S. aureus* contamination.

Conclusion:

Photocatalytic coatings reduced the bioburden of high-risk surfaces in the healthcare environment: treated surfaces became steadily cleaner, while untreated ones accumulated bioburden. This evaluation encourages a larger-scale investigation to ascertain whether the observed environmental amelioration has an effect on healthcare-acquired infection.

Introduction

Increasing microbial antibiotic resistance has given new impetus to keeping hospitals clean.[1] Hospital-acquired infection (HAI) is rightly seen as an unacceptable burden on the patient, as well as inflating hospital costs.[1] While there is general agreement on the need to control HAI, there is diversity of opinion regarding the best solution. A major problem is the difficulty of conclusively establishing a causal link between surface contamination and HAI[2], compounded by the lack of universally accepted standards for measuring cleanliness.[3] Nevertheless, it is plausible to assert that there is such a link[4], allowing us to debate the most cost-effective method for reducing contamination in the healthcare environment.

Current decontamination strategies include daily detergent- and disinfectant-based cleaning. Enhanced disinfection methods are available for rooms housing HAI patients and when an outbreak occurs.[5] Powerful disinfectants require caution, since few have been properly evaluated under actual conditions of use, and they may ultimately be no better than traditional detergent-based cleaning.[6,7] Manual cleaning has deficits, usually attributed to personnel rather than product, and recontamination inevitably begins immediately after the cleaning.[8,9]

Among recent technologies are photocatalytic antimicrobial coatings.[10] They kill microbes by generating powerful oxidizing radicals on a semiconductor surface following light absorption in the presence of O_2 and H_2O. The most important photocatalytic material is titanium dioxide (titania) because the bandgap of the semiconductor overlaps sufficiently with the spectrum of natural and common artificial light sources; the band edges are positioned appropriately for generating the radicals; and the material is stable with respect

to self-destruction.[10,11] The illuminated semiconductor acts as a source of reactive oxygen species (ROS), which are known to be highly effective microbicides[12]; the mechanism of antimicrobial destruction is believed to involve bacterial cell-wall damage.[13] Those ROS generated by illuminated titania are particularly reactive and it is thought that resistance against them cannot be developed.[12]

Although there have been *in vitro* investigations of photocatalytic antimicrobial action with titania, very little work in real-life situations has been reported.[10] A commercial titania coating (''EnviroCare") did not significantly prevent environmental microbial contamination.[14] This coating was, however, constituted from titania particles dispersed in a binder in order to ensure their attachment to the coated surfaces; the binder possibly encapsulated the particles and not only scavenged the photogenerated radicals but also formed a physical barrier between the particles and the microbes. Titania nanoparticles in suspension have been shown to be effective photocatalytic antimicrobial agents but they adhere very weakly to most surfaces[10,15], from which they would, therefore, be continuously lost. Petti and Messano dispersed titania nanoparticles in PVC and observed antimicrobial action on the surface of blocks made from the polymer[16], but this approach is obviously unsuitable for retrofitting to existing objects.

We resolved to evaluate a material (MVX) that is applied as a dilute aqueous sol of titania nanoparticles, which dries and gels to form a tough, adherent monolithic film on the coated surface. Given evidence that photocatalytic antimicrobial activity can be synergistically enhanced by the presence of copper or silver[11], we chose to use a product doped with a small proportion of silver zeolite. While it was tempting to coat all surfaces in a ward due to ease of application (by spraying), we focused on near-patient high-touch surfaces. They

were coated immediately after annual deep clean of the wards. Following the application, the microbial burden and associated pathogens were monitored over three months using standardized methods.

Setting

The coated bay was in an acute general medical ward, and an untreated control bay was selected in the stroke unit. The decision to spatially separate the treated and control bays, rather than having them in the same ward, was taken to avoid introducing a confounding factor in the form of a possible effect of the coating on resident staff hands, who potentially have access to all patients on the same ward. Both wards are located in a part of the hospital constructed in 2004, and are architecturally almost identical. The bays have a rectangular shape and a volume of approximately 144m^3. They are naturally ventilated with windows along one of the long sides facing north; artificial light is provided during waking hours (dimmed during the hours of sleep) from "daylight" fluorescent lamps. At patient level the illuminance was approximately 400lux.

Methods

Choice of surface sites for coating

It was decided to coat (i) left- and (ii) right-hand side rails of a standard hospital bed; (iii) the front face of the bed control panel; (iv) the top of the bedside table (v) the bedside locker (in entirety, but only the top was sampled); and (vi) the bed footboard (only the top was sampled). There is general consensus about the potential HAI risk from these sites.[17] The furniture (table and locker) was made from laminated wood. Each of these six sites was replicated for all four bedspaces occupying one bay of the selected ward.

Ward preparation

Prior to coating the wards were deep-cleaned, which comprises thorough cleaning with a 5000ppm solution of Actichlor Plus (Ecolab, UK) (a combination of a chlorine-compatible detergent with sodium dichloroisocyanurate, NaDCC, also known as troclosene sodium) followed by steam cleaning and, as a final step, enhanced cleaning with hydrogen peroxide vapour (HPV, Deprox; Specialist Hygiene Solutions Ltd, Kings Lynn, UK). The stroke ward was deep-cleaned in the week commencing 1 August 2016 and the acute medical ward was deep-cleaned in the week commencing 10 September. No patients were admitted to the ward between deep cleaning and coating.

Coating procedure

The coating is a dual one, comprising a colourless primer ("Primary") over which the photocatalytic titania coating ("MVX") is laid. Final coating thickness was approximately 1µm. The precursors are dilute aqueous solutions of the active ingredients, titania (1.5%) and silver zeolite (0.1%).[18] These solutions, as well as the final coating, are nontoxic to humans.[21] Primary (MVX Hitech Co. Ltd, Kitakyushu, Japan) was sprayed onto the selected surfaces and allowed to dry for 20–30min; the ambient temperature in the ward during coating was 26±1^{o}C and the relative humidity was 59±3%. Then MVX was applied likewise by spraying and similarly allowed to dry. After drying, the coating was invisible to the eye, even on mirrors (integral on some lockers). All coated objects were discreetly fitted with trackers for the TeleTracking Technologies (Pittsburgh, Pennsylvania) real-time location system (RTLS) installed at the hospital as part of the "Safe Hands" programme, to ensure that the coated objects could always be unambiguously located, even if clinical exigence (e.g., to

reduce the risk of falls, or simply to make the patient more visible) led to a patient (with bed and bedspace equipment/furniture) being moved, generally within the ward.

Sampling protocol

The approach followed that described in Bogusz et al.[19] Starting at 7am on Tuesdays and Thursdays, for 12 weeks (22 September–21 December 2016), after locating the objects with the RTLS, the coated sites and their uncoated equivalents were sampled using double-sided dipslides (Hygiena International, Watford, UK) coated with nutrient and Baird Parker agars, pressing the slides at 25g/cm^2 for 5s.[20] Within the sites, the actual locations were determined at random[21], according to the judgment of the (sole) sampler.

Microbiology

Dipslides were incubated for 48–72h at 36±1^{o}C according to laboratory protocol, after which the number of aerobic colony-forming units (cfu) was determined from the nutrient agar side. Baird Parker agar highlighted potential coagulase-positive staphylococci, which were subcultured onto blood agar and identified as methicillin-susceptible or -resistant according to laboratory protocol. The aerobic colony count (ACC) was quantified using a 5-point scale (Table 1).[3,7,19] Staphylococci were classified as either ‘’isolated” or “not isolated”.

Ward environment

Every day, the ward cleaning team cleaned all items in the patient bed space with Hospec general surface cleaner (containing alcohol ethoxylate as the detergent) (Robert McBride Ltd, UK), typically during the morning after sampling. No exceptional cleaning (HPV or Actichlor Plus) was requested for the control ward during the study. Actichlor Plus was

requested on three occasions in the treated ward, but for side rooms away from the treated bay. Unlike the strongly bactericidal ionic surfactants, nonionic surfactants are generally considered to be less bactericidal, although they interfere with bacterial membrane fluidity.[22] It is difficult to separate the physical bactericidal effect of the mechanical wiping action from the biochemical bactericidal effect associated with the surfactant[23], but some attempts at quantification have been made.[7,19]

Bed occupancy was high in both treated and control wards, averaging 97.6% for the former and 88.0% for the latter during the study (data for the entire ward). Locally agreed staffing levels are recorded for all wards at the hospital. The stroke ward was generally better staffed than the acute ward. Medical staff, allied health professionals (AHP, including physiotherapists, occupational therapists, speech and language therapists) and domestics were not included, nor were visitor numbers monitored.

The degree of dependency (acuity) of the patients occupying the beds was also examined. The median degree was invariably level 1b using the Hurst classification.[24]

The hospital R&D department determined not to class the study as research but rather as a service evaluation. Therefore, Research Ethics Committee approval was not required.

Statistical methods

The sampling protocol resulted in a maximum of 102 bedspace observations for each ward subsequently available for statistical analysis. Each observation produced six measurements of ACCs, which were allocated a numerical descriptor from 1 to 5 (Table 1). For the statistical analysis, a mean ‘’numerical descriptor” score (i.e., arithmetic mean of the six test sites) was calculated for each bedspace. This was dichotomized into a pass/fail outcome

variable (1–2 = ''pass" and >2–5 = ''fail"). Although dichotomizing may lead to a loss of statistical power,[25] it is in concordance with the previously introduced pass/fail dichotomy for bioburden.[3,26] Furthermore, the conventional classification (Table 1) gives a highly nonlinear mapping of ACCs onto a descriptor; by dichotomizing we avoid having to discuss whether to express the results in terms of cfu/cm^2 or in terms of the "degree of growth" descriptor.

The difference in pass/fail rate between the two wards (experimental and control) was assessed using the χ^2 independence test. Straightforward binary logistic regression analysis was used to further explore the probability (odds) of failing the pass/fail test on the two wards.[27] Additional factors (introduced as continuous covariates) included the number of days into the study (0–90) and the bed occupancy rate (%) for each ward. The multiple regression logit model was fitted using the binary logistic regression analysis option in SPSS (SPSS Inc., Chicago, Illinois). The analysis allows both fixed and categorical factors and continuous covariates to be used as explanatory variables when estimating the probability (or, more correctly, the odds) of failing the test. $P < 0.05$ was used as a measure of significance.

Results

The overall pass rate for the coated bay was 80.4% (82 passes out of a total of 102 samples), while for the control bay it was 52.9% (54 passes out of 102).

The results of the binary logistic regression analysis, using the control ward as the reference condition, are given in Table 2. The analysis identified no difference in the odds of failing the test between the two wards at the beginning of the experiment (odds ratio OR=0.993;

95%CI 0.267 to 3.69; *P* = 0.993). However, the odds of failing the test in the control bay increased by 2.6% per day (*B*=0.026), (OR=1.026; 95%CI 1.009 to 1.043; *P* = 0.003) but declined by 2.5% per day in the treated bay (*B*=0.026–0.051), (OR=0.95; 95%CI 0.925 to 0.977; *P* < 0.001). These trends are plotted in Figure 1.

For the individual sites, we considered the sampling as a sequence of independent Bernoulli trials with the binary outcome of ''pass" or ''fail" and an initially unknown probability *p* of passing, which was found from the maximum of the likelihood of *p*, given the observed sequence.[28] The results are given in Table 3. MVX significantly improved microbial cleanliness at every site, although only borderline significance was achieved for the bed footboard. The left-hand and right-hand bedrails were conceived as internal controls for each other, but yielded different ''pass" probabilities; there may have been physical differences in accessing the bedrails, such as one bedrail being closer to a wall or some other obstruction.

S. aureus was isolated from only about 10% of the dipslides: There were 97 isolates recovered from a total of 635 for the treated surfaces (all sites together), compared with 68 isolates from a total of 655 for the control surfaces. The low *S. aureus* counts render the difference insignificant.

Discussion

The gradual diminution of bioburden on the treated surfaces occurred although bed occupancy was higher than in the untreated bay, which would have likely encouraged heavier microbial contamination on ward surfaces.[26] This result implies that gradual removal

of the coating by mechanical abrasion from touching or cleaning, initially considered as a possibility, did not occur.

Among the possible confounding factors considered (Hawthorne effect; bed occupancy; staffing levels; and degree of patient dependency) only bed occupancy differed markedly between the treated and control bays. Although the patients differed between the two study bays, there was no evidence for a clinically significant difference with respect to the likelihood of individual patients and attendant staff contributing to the microbial burden in their environment.

Environmental audits undertaken to appraise housekeeping compliance with cleaning are reported in Table 4 for the interval of the study. They show little difference between the two wards.

It is interesting to compare the bioburden reduction provided by the photocatalytic coating with conventional detergent or disinfectant application to high-touch surfaces (UK hospitals, generally use detergents, and hospitals in the USA generally use disinfectants). Microbial counts from a wide range of hand-touch sites cleaned with detergent ranged from 2.5 to 40cfu/cm^2 [29]; detergent cleaning was shown to reduce bioburden from a preclean level of 6.7cfu/cm^2 to 3.5.[19] On the other hand, disinfectant reduced median counts for high-touch sites to 0.1–0.6cfu/cm^2.[30] A major difficulty is that sampling methods, surfaces, sites (near-patient hand-touch sites host different amounts and types of bioburden than floors or bathroom sites), cleaning agent exposure, and culture techniques are not standardized across studies. Another confounding factor is sampling methodology: greater quantities of

bioburden are recovered from moistened swabs placed in broth then agar methods such as RODAC plates or dipslides.

Our results suggest that the chosen wards were already rather clean, especially with respect to *S. aureus*; the effect of the photocatalytic coating in lowering bioburden might be more prominent in a less stringently clean hospital. Conversely, a recent study of the effect of MVX in the critical care environment, which is always afforded priority for cleaning (e.g., routinely cleaned with alcohol thrice daily) found no significant microbiological benefit, despite *in vitro* data from the same coating showing pathogen inactivation.[31] The duration of the study was only 4 weeks, however, which may anyway be inadequate to provide sufficient statistical power to show any significant difference between treatment and control.

Although a photocatalytic surface continuously maintains its antimicrobial action, the action is fairly slow. Kinetic laboratory studies, in which surfaces were deliberately contaminated with known amounts of bacteria, suggest that about one hour is needed to destroy half the bacteria.[32,33] Hence, if a site had been adventitiously heavily contaminated a few minutes prior to sampling, the result would indicate a high bioburden, whereas sampling two hours later might indicate low contamination.

The ultimate objective for hospitals regarding cleanliness is to reduce the incidence of HAI. At present the relationship between microbial burden on hospital surfaces and the incidence of HAI remains unclear; no extant model allows one to predict the change in HAI incidence as a result of lowering environmental bioburden by a defined amount, and so far no empirical study appears to have tackled this deficit. A few studies have examined the link

between standardized measurements of bioburden and HAI rates, but with inconclusive outcomes.[2] Much attention has been given to the proposition that hands are the main vectors for transmission and, therefore, that frequent hand hygiene is the key to reducing HAI, although the limitations of this approach were noted decades ago.[34] Furthermore, although hand hygiene is strongly promoted in the healthcare setting, compliance is still far from what is considered to be ideal but may nevertheless have already reached a practical limit.[35] In any case, hand contamination is most likely to be transmitted via the intermediary of high-touch surfaces, such as those investigated in the present study, rather than directly to another hand.

"Routine cleaning and disinfection is apparently not sufficient".[36] Detailed investigation of routine processes may reveal weaknesses, in addition to those already discussed, alongside their irreducible intermittency.[9,37] In contrast, a photocatalytic surface is continuously active. Some of the physicochemical changes induced in titania by light persist for many hours or days in the dark, reinforcing this continuity.[38] A photocatalytic coating of the type evaluated here offers a new perspective for overcoming some of the present limitations in cleaning, disinfection, and hand hygiene. A further advantage is that the mechanism whereby photocatalytic antimicrobial coatings inactivate microbes is unlikely to lead to the development of resistance,[12] the increase of which is of grave concern to public health authorities.

In conclusion, coating high-touch surfaces with a titania-based photocatalytic material significantly lowered bioburden compared with a control bay. The trend of continuously diminishing bioburden in the treated bay is encouraging, not least in comparison with the untreated control bay, in which the bioburden appeared to continuously increase. A much

larger and longer study should now be undertaken with sufficient power to observe whether coating high-touch surfaces with an antimicrobial coating reduces the incidence of HAI. Although there is no evidence that non-touch surfaces (walls, ceilings, etc.) are reservoirs for microbes, empirically verifying or otherwise the proposition that coating *all* surfaces with a photocatalytic material reduces the incidence of HAI will be a further useful addition to knowledge.

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Table 1: Classification of aerobic colony counts (ACCs).

cfu/cm^2	Name	Numerical descriptor	Binary score[a]
0	No growth	1	Pass = 1
<2.5	Very slight growth	2	Pass = 1
2.5 – 12	Light growth	3	Fail = 0
12 – 40	Moderate growth	4	Fail = 0
> 40	Heavy growth	5	Fail = 0

[a] According to Dancer (2008).[26]

Table 2: Factors (variables) found to influence the probability *p* of failing the test, estimated using binary logistic regression, adopting (fail v. pass) as the dichotomous response variable: Estimated parameters B_i for the logit model [$\log[p/(1-p)]=\text{Constant} + B_i$**], where the subscript *i*=1 refers to the untreated sites and *i*=2 to the treated ones.**[e]

	B[a] (SE)	*P*[b]	OR[c]	95% CI[d]	
				Lower	Upper
Control ward	0.000		1.00		
Treated ward	–0.007 (0.670)	0.991	0.993	0.267	3.690
Days into the evaluation (for the control ward)	0.026 (0.009)	0.003	1.026	1.009	1.043
Treated ward-by-days	–0.051 (0.014)	0.000	0.950	0.925	0.977
Bed occupancy (%)	0.076 (0.034)	0.026	1.079	1.009	1.154
Constant	–7.866 (3.099)	0.011	0.000		

[a] Slope parameter of the continuous covariate (days), with its standard error in parentheses.

[b] Measure of significance.

[c] Odds ratio, equal to exp(*B*).

[d] Confidence intervals for exp(*B*).

[e] The control ward was estimated as the baseline constant parameter (at day zero) and the treated ward effect was estimated as a deviation from this constant parameter. The number of days from day zero and bed occupancy were introduced as continuous covariates.

Table 3: Success probabilities *p* for the (lack of) aerobic growth at the various sites.

Site	*p*		Number of observations		*s* [a]		$\lvert p_{treated} - p_{control} \rvert / (s_{treated} + s_{control})$ [b]
	Treated	Control	Treated	Control	Treated	Control	
Left side bedrail	0.66	0.51	98	102	0.05	0.05	1.5
Right side bedrail	0.82	0.44	98	102	0.04	0.05	4.2
Control panel	0.80	0.73	99	97	0.04	0.05	0.8
Bedside table	0.86	0.75	99	95	0.03	0.04	1.6
Bedside locker	0.95	0.79	87	102	0.02	0.04	2.7
Bed footboard	0.51	0.48	87	91	0.05	0.05	0.3
All sites	0.77	0.61	568	577	0.018	0.020	4.2

[a] The span *s* is the square root of the observed formation, which is a measure of the uncertainty of *p*. [28]

[b] The difference between the probabilities divided by the sum of the spans is an index of the significance of the result: the greater the index, the greater the significance.

Table 4: Environmental audits for housekeeping compliance with cleaning.[a]

Month	Monthly "Health Assure" environmental audit scores		Monthly "Credits for Cleaning" (C4C) environmental audit scores	
	Treated ward	Control	Treated ward	Control
September	98.2%	93.6%	99.5% [b]	98.1% [b]
October	99.1%	84.0%	98.4% [c]	99.4% [c]
November	98.2%	87.0%	99.0% [d]	97.7% [d]
December	90.0%	84.6%	98.8% [e]	99.6% [e]

a The audits do not directly observe the staff actually cleaning but inspect the whole ward environment, including high-touch surfaces.

[b] Week commencing 19 September.

[c] Week commencing 24 October.

[d] Week commencing 28 November.

[e] Week commencing 9 January.

FIGURE LEGEND

Figure 1. Actual data (open circles) and predicted values (open triangles) for the control sites and treated sites (data: closed blue-grey circles; predicted values: closed triangles) for the duration of the evaluation. The vertical axis is microbial growth according to the 5-point scale (Table 1).